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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,085	03/15/2004	Eifion Phillips	A1695-5P US	9462

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
06/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,085	PHILLIPS ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-8 and 18-20* is/are allowed.

6)☒ Claim(s) *9,10,16 and 17* is/are rejected.

7)☒ Claim(s) *11-15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-20 are now pending in the instant application.

Response to Amendment

2. Receipt is acknowledged of Applicants' Amendment and Response, submitted March 26, 2007, which has been reviewed by the Examiner and entered of record in the file. Accordingly, claim 19 has been amended and new claim 20 has been added.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9-17 previously rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, and the *In re Wands* factors (cited in the previous office action) have been applied. Applicants traverse the rejection, arguing that the Examiner has not provided sufficient guidance as to the conditions or disorders that are enabled. Applicants also contend that, "... the specification is enabling for treating all conditions mentioned and that the quantity of experimentation is no undue.... Additionally, with the guidance provided in the specification those skilled in the art would know how to determine the binding properties of a compound of Formula I and would appreciate that a compound having such binding activity would interact with nicotinic acetylcholine receptors and would be useful in the treatment of the named disorders."

The Examiner respectfully disagrees, and directs Applicants' attention to page 1 of the specification wherein a few journal articles and patents that teach compounds with similar

nAChR binding activity are referenced in lines 16-32. Namely, similar compounds are discussed that show efficacy for treating conditions and disorders such as learning deficit, cognition deficit, attention deficit, memory loss, ADHD, manic depression, mania, anxiety, schizophrenia, jetlag, smoking cessation, nicotine addiction, certain types of pain, and ulcerative colitis.

While the Examiner agrees that Applicants are enabled for treating certain diseases, conditions, or disorders, she maintains that Applicants have still not provided sufficient data to enable the treatment of the full range of diseases, conditions, or disorders that are encompassed by the claim language, "... a condition or disorder arising from dysfunction of nicotinic acetylcholine receptor neurotransmission" of claims 9 and 10 or any neurodegenerative disorders recited in claims 16 and 17. The argument that all of the diseases or conditions claimed involve reduced cholinergic function and therefore can all be treated by compounds that bind nAChR's is insufficient evidence given the broad range of unrelated diseases/disorders. Regarding the treatment or prevention of neurodegenerative diseases including Alzheimer's disease, Applicants have not shown that the instant compounds are beneficial for treating *all* types of neurodegenerative disorders or conditions. The broadly claimed "neurodegenerative conditions" includes many disorders that are extremely difficult to treat and have no known cure, such as Alzheimer's disease, Parkinson's disease, Motor Neuron disease, Huntington's disease, MS, and stroke. Applicants provide only a few *in vitro* binding assays on pages 23-24, which are not sufficient evidence for treating all known neurodegenerative conditions, particularly given their complexity and unknown causes (please refer to the attached internet article, "Alzheimer's Disease, Parkinson's Disease and Related Brain Disorders: Brief Overview for Patients and Caregivers").

Regarding the term "or preventing," even if the patient has a genetic predisposition to the selected identified disease states, one is still treating the individual patient, and not preventing. It has not been shown in the specification that the absolute "**prevention**" of such disease is accepted in the art as being predictive of the utility alleged, especially when absent of pharmacological data. The diseases that the instant claimed compound is enabled for treating include neurodegenerative diseases. Although the clinical and neuropathological aspects of these diseases are distinct, their unifying feature is that each disease has a characteristic pattern of neuronal degeneration in anatomically or functionally related regions. Presently available pharmacological treatments for the neurodegenerative disorders are symptomatic and do not alter the course of or progression of the underlying disease (see Goodman and Gilman's, The Pharmacological Basis of Therapeutics, 10th Edition, page, 549). Therefore, the state of the art is limited to treatment of said diseases and not the prevention of said diseases.

Because of high level of unpredictability associated with **"prevention"** of certain diseases such as dementia, mania, or schizophrenia, a greater amount of evidentiary support is needed to fully satisfy the requirement of 35 U.S.C 112, first paragraph. It is noted that pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities.

The specification discloses methods of treating diseases such as psychotic disorders and intellectual impairment disorders, using the compounds described in the specification. The

compounds that are disclosed in the specification, which have data regarding the claimed compounds' affinity of the α_4 and α_7 nAChR subtypes, have no pharmacological data regarding the prevention of said diseases. The specification is short of any working data (animal models or *in vivo* testing) in regards to the prevention of said diseases. Merely stating that the instant compounds are preventable against, for example manic depression, does not establish usefulness of the invention absent art-recognized correlation between such tests and the ultimate use.

A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that compounds fall within the scope of a claim will posses the alleged activity. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F2d 349, 151 USPQ 724. The instant specification at most only provides examples of intermediates and processes of preparation. No examples have been set forth describing the prevention of said diseases. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds would prevent the claimed diseases.

It is suggested to delete the terms "or preventing" to overcome the rejection.

Thus, the specification fails to provide sufficient support of the broad use of the compounds for the treatment or prevention of <u>all</u> disorders encompassed by claims 9 and 10, as well as neurodegenerative conditions (Alzheimer's, etc) of claims 16 and 17.

The remaining method of use claims 11-15 are objected to as being dependent on rejected base claims.

5. Claim 19 previously rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of Applicants' amendatory changes to the claims, the indefiniteness rejection is withdrawn.

Conclusion

6. Claims 1-20 are pending in the application, claims 1-8 and 18 appear to be in condition for allowance, claims 11-15 are objected to, and claims 9, 10, 16 and 17 stand rejected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Coppins
June 10, 2007

Joseph K. McKane
SPE, Art Unit 1626